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19. ABSTRACT (Continue on reverse if necessary and identify by block number) Complexation of the (R)- and (S)- forms of α -(1-naphthyl)ethylammonium perchlorate by chiral pyridino-18-crown-6 ligands 1-6 (Figure 1) has been studied by the temperature dependent ^1H NMR technique. ¹ At low temperatures, the peaks in the ^1H NMR spectra of the complexes attributable to the hydrogen atoms on the CH_2 groups attached to the pyridine rings (centered at about 4.5), or the methyl hydrogens in the cases of 5 and 6, separated into two peaks of equal intensities. The low temperature peak separations were 40-140 Hz. At high temperatures, the appearance of a single peak is caused by a fast intermolecular or intramolecular face to face guest exchange. The kinetic parameters for the dissociation of these complexes were calculated as reported. ¹ Table I shows the differences in ΔG_c^\ddagger for the dissociation of the complexes of 1-6 with (R) and (S)- α -(1-naphthyl)ethylammonium perchlorate. It				
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is evident from these differences in the ΔG_c^\ddagger values in Table I that these chiral ligands exhibit enantiomeric recognition.

Also in Table I, these $\Delta \Delta G_c^\ddagger$ values are compared with those calculated from the conformational equilibrium energies of the complexes.^{2,3} These calculated energies included those for the ion-ligand interactions and the strain energy of the ligands that are the main components of ΔG_c^\ddagger . They are therefore the main contributors to $\Delta \Delta G_c^\ddagger$. The other components that are temperature or solvent dependent are smaller and not much different for the (R) and (S) complex and therefore are mostly cancelled out in the calculated $\Delta \Delta G_c^\ddagger$ values.^{1,2} Consequently, the calculated energy difference represents approximately the $\Delta \Delta G_c^\ddagger$ value.

The computer-calculated $\Delta \Delta G_c^\ddagger$ values for the complexes of ligands 1, 3, 4 and 6 with the salt were about the same as those determined by the ¹H NMR method. The calculated $\Delta \Delta G_c^\ddagger$ values for the complexes of 2 and 5 were significantly higher than the determined values. Based on this significant, though less than thorough, agreement between the determined and calculated values of $\Delta \Delta G_c^\ddagger$ for some of these complexes, the force field calculations were further extended to many other variants of the same family of molecules such as 7 and 8. The calculations were used to estimate the expected capacity of these variants for enantiomeric recognition, and helped to choose which variants should be synthesized and which should not. Thus, the variant with R₁ = t-butyl is predicted to yield high enantiomeric recognition, and is currently being prepared in our laboratory. Other variants where R₁ = other alkyl groups were shown to be less promising, and are not being prepared.

The computer-generated stereoviews of the ligand-ion complexes complemented the calculated $\Delta \Delta G_c^\ddagger$ values by exposing visually the nature of the ion-ligand interactions and the source of the enantiomeric recognition. Figure 2 represents stereoviews of the two diastereoisomeric ion complexes with ligand 8 each viewed from two perpendicular directions. It is seen that for the (R)-enantiomer, the t-butyl substituent contacts the methyl part of the salt, the naphthyl substituent of the salt contacts the pyridine, and the three NH bonds are properly oriented towards their respective ligating groups, thus optimizing the salt-ligand electrostatic interaction. The (S) enantiomeric salt appears to be less favorably bound to the ligand. The naphthyl substituent of the salt repels the t-butyl substituent of the ligand, thus introducing distortion and strain in the complex, and the NH bonds are not well oriented towards their respective ligating group, thus weakening the salt-ligand interaction.

1. Davidson, R. B.; Bradshaw, J. S.; Jones, B. A.; Dalley, N. K.; Christensen, J. J.; Izatt, R. M. Izatt, R. M.; Morin, F. G.; Grant, D. M. J. Org. Chem. 1984, 49, 353.
2. Lifson, S.; Felder, C. E.; Shanzer, A. J. Am. Chem. Soc. 1983, 105, 3866.
3. Lifson, S.; Felder, C. E.; Shanzer, A.; Libman, J. in "Progress in Macrocyclic Chemistry," Vol. 3, Izatt, R. M.; Christensen, J. J. Eds., Wiley Interscience, New York, pp. 241-308, 1987.

Table I. Differences in Free Energies of Activation ($\Delta\Delta G_c^\ddagger$, kcal/mol) $[\Delta G_c^\ddagger(R) - \Delta G_c^\ddagger(S)]$ for the Interaction of Various Chiral Macrocyclic Ligands with (R)- and (S)- α -(1-Naphthyl)ethylammonium Perchlorate (A in Table I) as Determined Experimentally (NMR) and as Calculated from Empirical Energy Functions^a.

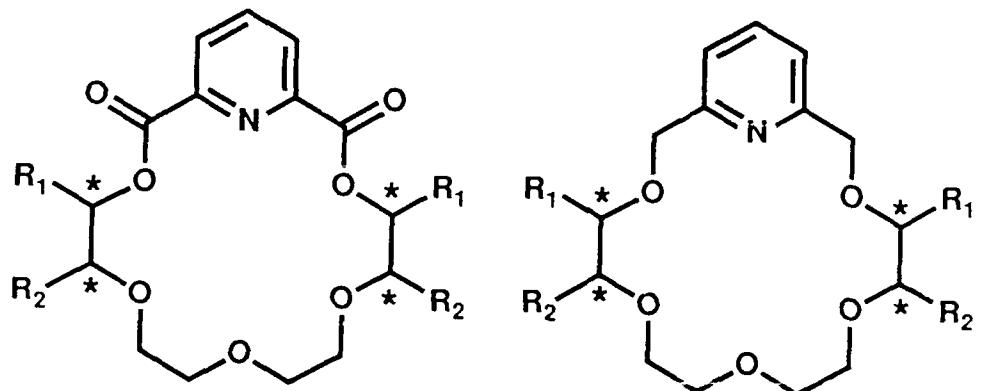
Ligand	$\Delta\Delta G_c^\ddagger$	
	Determined	Calculated
(S,S)-1	1.1 ^b	0.7
(S,S)-2	1.3	2.5
(S,S)-3	0.1 ^b	0.1
(S,S)-4	1.6 ^b	1.7
(R,R)-5	0.8	1.7
(R,R,R,R)-6	0.9	0.9
7, R = t-butyl (Y = O)		2.5
8, R = t-butyl (Y = H ₂)		2.2

^aEmpirical calculations as reported in references 2 and 3. ^bData from reference 1.

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Figure 1. Chiral Pyridino-18-Crown-6 Ligands



1, $R_1 = CH_3$; $R_2 = H$
(S,S) & (R,R)

2, $R_1 = C_6H_5$; $R_2 = H$
(S,S)

3, $R_1 = H$; $R_2 = C_6H_5$
(S,S)

7, $R_1 = C(CH_3)_3$, $R_2 = H$

4, $R_1 = CH_3$; $R_2 = H$
(S,S)

5, $R_1 = CH(CH_3)CH_2CH_3$;
 $R_2 = H$ (R,R)

6, $R_1, R_2 = CH_3$;
(R,R,R,R)

8, $R_1 = C(CH_3)_3$, $R_2 = H$

Figure 2. Computer-Generated Stereoviews Obtained From Force Field Calculations of the Complexes of the Proposed (S,S)-Di-*t*-butyl-Substituted Pyridino-18-Crown-6 with (R)-*alpha*-(1-Naphthyl)ethylammonium Perchlorate (Stereoviews A) and With the (S)-Perchlorate (Stereoviews B)

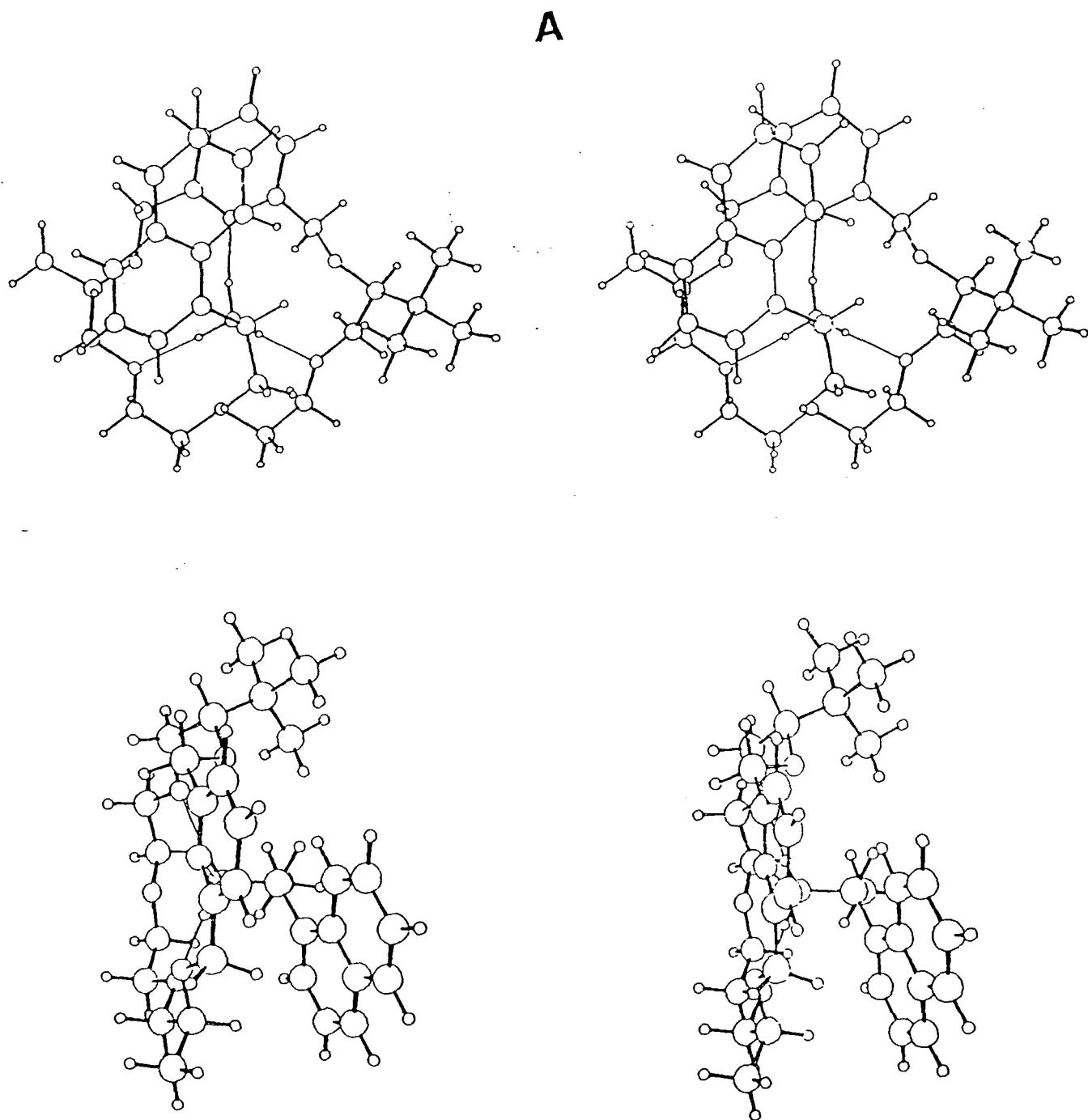


Figure 2. (Continued)

B

